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The Influence of Exercise on Cardiovascular Health in Sedentary Adults with HIV

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Abstract

Background—Lifestyle physical activity (i.e. moderate physical activity during routine daily activities most days of the week) may benefit HIV-positive adults who are at high risk for cardiovascular disease.

Objective—To describe lifestyle physical activity patterns in HIV-positive adults and to examine the influence of lifestyle physical activity on markers of cardiovascular health. Our secondary

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objective was to compare these relationships between HIV-positive adults and well-matched HIV-uninfected adults.

Methods—One-hundred and nine HIV-positive adults and 20 control participants wore an ActiGraph accelerometer, completed a maximal graded cardiopulmonary exercise test, a coronary CT, anthropomorphic measures, and had lipids and measures of insulin resistance measured from peripheral blood.

Results—Participants (n=129) had a mean age of 52 (±7.3) years, 64% were male (n=82), and 88% African American (n=112 of 129). On average, HIV-positive participants engaged in 33 minutes of moderate-to-vigorous physical activity per day (IQR: 17, 55) compared to 48 minutes in controls (IQR 30,62; p=0.05). HIV-POSITIVE adults had poor fitness (VO_2 peak: 16.8 (±5.2) ml/min/kg and VE/VCO_2: 33.1 (4.6). A marker of HIV disease (current CD4+ T cell) was associated with reduced VO_2peak (r=−0.20; p<0.05) and increased insulin resistance (r=0.25, p<0.01), but not with physical activity or other markers of cardiovascular health (p's≥0.05). After controlling for age, gender, BMI, and HIV status, physical activity was not significantly associated with VO_2 peak or VE/VCO_2.

Conclusions—HIV-positive adults have poor physical activity patterns and diminished cardiovascular health. Future longitudinal studies should examine whether HIV infection blunts the beneficial effects of physical activity on cardiovascular health.

Keywords

HIV; Exercise; Cardiovascular Diseases; Exercise Test

Approximately 1.2 million people are living with HIV (PLWH) in the United States, and there are over 30 million PLWH worldwide. HIV antiretroviral therapy (ART) has significantly increased the life expectancy among PLWH.[1,2] Long term HIV infection, HIV treatment, and lifestyle factors have led to PLWH experiencing age-related comorbid conditions earlier and more frequently than HIV-uninfected individuals.[3] Specifically, PLWH experience chronic inflammation, long-term use of ART, and higher rates of lifestyle risk factors which increase their risk for cardiovascular disease (CVD)[3] and create an urgent need for interventions that reduce this risk.

Physical activity includes activities performed as part of daily life (e.g. walking), as well as planned, more vigorous physical activity.[4] Seminal research has shown that physical activity can improve cardiovascular and metabolic health.[5] Conversely, physical inactivity is associated with poor glycemic control and reduced triglyceride clearance, resulting in an increased risk of mortality and cardiometabolic complications.[6] Further, PLWH also have higher rates of insulin resistance, fatigue, pain, depression, and smoking and alcohol use, compounding their risk for CVD.[7–13] PLWH can benefit tremendously from physical activity, but their objectively-measured physical activity patterns, and the influence of those patterns on cardiovascular health, are not well understood. The aims of this study were to describe physical activity patterns in PLWH who did not meet AHA recommended guidelines for physical activity, and to examine the relationship of these patterns to markers of cardiovascular health. Furthermore, we aimed to compare these relationships between PLWH and a well-matched HIV-uninfected control group.

METHODS

Design

These data derive from a cross-sectional analysis of baseline data from a clinical trial (parent study) testing the effect of a self-management intervention on exercise and cardiovascular outcomes in a group of PLWH, compared with well-matched HIV-uninfected control participants (NCT02553291).

Sample and Recruitment

One-hundred and nine PLWH and 20 well-matched control participants were recruited via IRB-approved letters to an HIV research registry and flyers posted in HIV care organizations in Cleveland, Ohio. HIV uninfected participants were recruited using ResearchMatch and flyers posted in primary care clinics in Cleveland, Ohio. Those interested in participating telephoned a Research Assistant who screened callers for eligibility. HIV-uninfected participants were matched to PLWH on race, sex, age (± 3years). All participants had to be >18 years of age and at high risk for developing CVD (Framingham 30-year CVD risk score>20% for females and >30% for males). If prescribed a statin medication, participants had to be taking it for at least 6 months. Additionally, PLWH had to be on antiretroviral therapy with suppressed HIV-1 viremia (<400 copies/mL) for at least one year prior to enrollment. Potential participants were excluded if they: 1) had a medical contraindication for exercise,[14] 2) met weekly physical activity recommendations of 150 minutes of moderate-to-vigorous physical activity[15] (assessed using the 7-day physical activity recall[16]), 3) were unable to understand spoken English, 4) expected to move out of the immediate area, have surgery or were pregnant or planned on becoming pregnant in the next 6 months, 5) were diabetic (hgA1c>7%), or 6) were enrolled in a weight loss program.

Eligible participants were invited to an initial visit where study staff reviewed study purpose, procedures, risk and potential benefits with them. After confirming understanding, those wishing to proceed signed an informed consent document, completed a blood draw and, if a woman of childbearing age, a urine pregnancy test. The IRB at University Hospitals, Cleveland Medical Center approved this study.

Procedures and Measures

Demographics and HIV Characteristics—All participants completed a self-reported demographic survey assessing gender, race, education and monthly income.[17] A research assistant helped those who were unable to complete the self-administered computer survey. Participants also consented to medical chart abstraction from which study staff abstracted medical data including years living with HIV, current CD4+ T cell count and CD4+ T cell nadir.

Physical Activity—Participants were given an ActiGraph GT3X/+ accelerometer (ActiGraph, LLC, Fort Walton Beach, FL).[18–20] Participants were instructed to wear the accelerometer during all waking hours for 7 consecutive days, except for when showering and swimming. A research assistant affixed the monitor to adjustable elastic belts and placed it over the participant's non-dominant hip, and counseled the participant on the importance

of wearing it every day. A research assistant called each participant two days after they received the devices to check if they were wearing them correctly, address concerns, and remind them return it in one week. When participants returned the accelerometer, we checked to ensure that data met the minimum quality standards (at least 3 days and at least 10 hours per day).[21–23] Those not meeting standards were asked to re-wear it for 7 days. Accelerometer data were processed according to recommendations for adults and were sampled at 30Hz, using 60 second epochs and the normal filter.[24] Consistent with Caspersen's (1985) definition, activity ≥ 2 metabolic equivalents (METS) and ≥ 10 minutes was defined as exercise.[25] We used the ActiLife software to calculate the amount of time spent in light, moderate, vigorous and moderate-to-vigorous physical activity per valid day using the Freedson (1998) adult calculation.[26,27]

Blood Pressure and Body Mass Index (BMI)—Participants were escorted to a clinical research unit where trained research nurses measured their height, weight, and vital signs. Each participant's height was measured to the nearest 0.1cm by asking him or her to stand straight up against a stadiometer platform with shoes off. After removing everything but a light layer of clothing, the participant stepped on a scale and weight was measured to the nearest kilogram. BMI was calculated by dividing weight in kilograms by height in meters squared.

Cardiovascular Health—Our measures of cardiovascular health included cardiorespiratory fitness, cardiometabolic health indicators (see serum laboratory measures), and cardiac computed tomography (CT) scans. Cardiopulmonary exercise tests were performed using a computer-controlled Lodi bicycle ergometer (Groninger, Netherlands) with a MGC Diagnostics Cardiopulmonary Express system (MGC Diagnostics, St. Paul, MN). A trained investigator performed all of the tests using a 20 watt/minute ramp protocol. We measured cardiorespiratory fitness using a peak oxygen uptake (peak VO_2) measure. Peak VO_2 was defined as the maximal value of VO_2 during the final 30 seconds of exercise. The Wasserman-Hansen equation[28] was used to determine the percent of predicted peak VO_2. Ventilatory efficiency (VE/VCO_2 slope) was determined by the linear regression slope of the minute ventilation (VE) and VCO_2.[29] Anaerobic threshold was manually calculated using the Beaver-Wasserman V-slope method.[30]

All participants underwent a non-contrast CT scan of the chest for coronary artery calcium scoring. A single reader (blinded to treatment assignment and participant characteristics) quantified total coronary calcium score using the Agatston method.[31] All scans were performed on a 64-slice multidetector CT scanner (Somatom Sensation 64, Siemens Medical Solutions USA) with 30×0.6mm collimation, 330ms rotation time, and 120kV tube voltage. Three-millimeter slices were obtained from the carina to the diaphragm with prospective ECG gating at 60% of the R-R interval. Calcified coronary lesions were defined as areas of ≥6 pixels with density >130 Hounsfield units (HU).

Serum Laboratory Measures

Serum studies were used to evaluate cardiometabolic health indicators and inflammation. All participants underwent a 12-hour fasting blood draw at the clinical research unit where a

trained phlebotomist drew approximately 20 mL of blood. Serum measures of HgA1c, glucose, insulin, and hsCRP were analyzed fresh samples using standard clinical procedures and commercially available assays at the hospitals lab. We used participants' fasting glucose and insulin measures to calculate the homeostatic model assessment of insulin resistance (HOMA-IR) for each individual.[32] IL-6 levels were measured in batch from plasma stored at −80 degrees C using the IL-6 Quantikine HS ELISA Kit from R&D Systems, INC (Minneapolis, MN). All assays were conducted according to the manufactures' instructions.

DATA ANALYSIS

All statistical analyses were performed using Stata version 14.0 (College Station, Texas). Data were cleaned and met assumptions for inferential statistics. We analyzed demographic, HIV, physical activity and cardiovascular health characteristics by decade of age and HIV status. Categorical variables were summarized using frequencies and percentages. Continuous variables, depending on their distribution, were summarized with either means and standard deviations or medians and interquartile ranges. We used Pearson's correlation coefficient to analyze the relationships between physical activity and cardiovascular health, as well as HIV biomarkers in the PLWH. We used adjusted linear regression to identify independent associations between physical activity, cardiovascular health indicators, and HIV status. We adjusted for clinically relevant covariates known to influence these relationships, including age, gender, BMI, and IL-6.[33]

RESULTS

Demographics and HIV Characteristics

A total of 109 PLWH and 20 well-matched HIV uninfected participants were enrolled in the study. Among PLWH, 70 (64%) were male, 94 (86%) were African American, 56 (51% had a high school degree or less education, and 9 (8%) were employed. PLWH were less likely to be employed (8% vs. 35%), engage in less moderate daily physical activity (33.3 vs 47.8 minutes), had less ventilatory efficiency (33.1 vs. 30.2), and had a lower systolic blood pressure (124 mmHg vs132 mmHG), compared to the controls. Otherwise, there were no statistically significant differences between the two groups. Demographic, HIV and inflammatory characteristics are summarized in Table 1.

Physical Activity

A total of 90 PLWH (83%) and 19 (95%) control participants engaged in any moderate-to-vigorous physical activity (MVPA) in the past week. The median engagement in MVPA per day was 35.1 (IQR: 18, 58) minutes in PLWH and 55.2 (IQR 31,65; p=0.06) in controls. Nearly all physical activity was done at moderate intensity.

Cardiovascular Health

The average peak VO_2 achieved (mL/kg/min) for PLWH was 16.8 (±5.2) vs 16.9 (±5.9) for the control group.$VE/VC0_2$ for PLWH was 33.1 (4.6) compared to 30.2 (2.5) for the control group. In contrast to exercise, peak VO_2 achieved didn't change with age (Figure 1). Forty (36%) PLWH had a coronary calcium score greater than 1 compared to 8 (40%) in the

control group (Table 1). Among PLWH, step counts were associated with decreased IL-6 (r=−0.266, p<0.05), improved VO_2peak (r=0.342, p<0.05), and reduced insulin resistance (r=−0.215, p<0.05). There were no other associations between physical activity and markers of cardiovascular health.

Current CD4+ T cell count and CD4+ T cell nadir are important health indicators for PLWH, but were not associated with physical activity. However, current CD4+T cell count was associated with reduced VO_2peak (r=−0.199, p<0.05) and elevated insulin resistance (r=0.248, p<0.05) (Table 2).

The regression analyses indicated that (controlling for age, gender, BMI, and IL-6), physical activity was not significantly associated VO_2 peak (Overall Model Adjusted R^2=0.42, p<0.01), peak $VE/VC0_2$ (Table 3) or coronary calcium score (not shown). However, PLWH exhibited less ventilatory efficiency than controls and our interaction coefficient (β=−1.944, p=0.317) suggests that physical activity may help to mitigate this decreased ventilator efficiency (Table 3).

DISCUSSION

Our study is among the first to prospectively examine the relationships between objectively-measured lifestyle physical activity and cardiovascular health in PLWH compared HIV-uninfected controls. We produced several important findings in this study: (1) PLWH engaged in low amounts of physical activity, (2) PLWH achieved low levels of peak VO_2 and elevated levels of VE/VCO_2, suggesting that HIV may attenuate the effects of physical activity on cardiovascular fitness, and (3) HIV biomarkers (CD4+ T cells and CD4+ T cell nadir) were not associated with physical activity but were associated with peak VO_2 achieved. Furthermore, as our sample was largely African American, our work provides evidence that should be considered when developing targeted interventions to this high-risk and often underserved group.

While PLWH engaged in a median of 35 minutes of moderate activity per day, exceeding daily AHA recommendations, almost no one who engaged in vigorous activity suggesting that this is not exercise but rather activity conducted in the course of their activities of daily living. Our results are similar to those in a recent meta-analysis conducted by Vancampfort et al.[34] The authors examined self-reported physical activity levels using MET minutes per week in 3,780 PLWH.[34] They found that PLWH engaged in mostly light activity (72.8 min/week), followed by moderate (61 min/week), and vigorous activity (12.4 min/week). Approximately 50% of PLWH met recommended physical activity levels (≥150 min/week of MVPA) and no comparisons were made to controls.[34] Conversely, in the Multicenter AIDS Cohort Study (MACS),[35] physical activity levels of PLWH and non-infected controls (n=1,281) were measured using the International Physical Activity Questionnaire (IPAQ).[36] Compared to Vancampfort's et al. and our results, they found that PLWH engaged in higher levels of MVPA and physical activity behaviors were similar to controls.[35] Among MACS participants, HIV infection and low levels of physical activity were associated with higher insulin resistance, further demonstrating the importance of physical activity to cardiometabolic health in PLWH.[35,37]

Our results build on previous research by providing both objectively-measured physical activity and a well-matched comparison group. The total amount of MVPA our participants engaged in was approximately 30% less that that reported by controls or by MVPA totals in Vancamfort et al's (2017) review. There are several possible explanations for our comparatively low level of physical activity. First, by using an ActiGraphs, we minimized the risk of over-reporting and behavior change bias associated with visual feedback seen in other wearable devices.[38] Second, we enrolled participants who did not meet physical activity recommendations to target those most likely to benefit from an intervention. This may have blunted the overall amount of observed physical activity. However, of the 204 participants screened for this study, only 10 were excluded because they exceeded weekly physical activity recommendations. It is possible that while low, the physical activity patterns observed in our study may be reflective of the PLWH ages 40 and older. Finally, our sample is older than those previously analyzed, and physical activity levels decrease as PLWH age, highlighting the need for increased physical activity interventions in older PLWH.

Given these low levels of physical activity, it was unsurprising to find that some cardiovascular parameters of health were lower in PLWH compared with healthy controls. The peak VO_2 achieved for all PLWH was 16.8 ml/min/kg (±5.2) and the VE/VCO_2 was 33.1, indicating impaired CO_2 removal and a higher risk for heart failure-related mortality.[39] Peak VO_2 declined and VE/VCO_2 increased with age. Similarly, Vancamfort et al. (2016) found that the average peak VO_2 among PLWH was 26.4 ml/min/kg, among the lowest levels of those living with chronic diseases.[40] Further, the average VO_2 peak among healthy adults was 34 (ages 40–59) ml/min/kg ,[41] significantly higher that our observed values. These data suggest that PLWH have poor cardiovascular fitness, which may underlie much of the increased CVD burden experienced by this population. These data also illustrate the critical importance of assessing cardiovascular fitness in this population both clinically and as a research variable.[42]

Cardiovascular health can be improved though regular, moderate-to-vigorous lifestyle physical activity. Recently, O'Brien et al.[10] found that combined aerobic and resistance interventions at least three times per week for at least five weeks can significantly improve cardiorespiratory fitness (Peak VO_2 $\Delta \geq 2$ mL/min/kg). However, studies testing home-based interventions among PLWH have largely been unsuccessful, failing to produce meaningful change in physical activity in this population.[43–45] This suggests that these interventions were not well targeted to PLWH. Additional, rigorous, developmental research is needed to better understand how to improve physical activity in this population.

Finally, we observed a relationship between CD4+T cell count and VO_2peak (r=−0.199, p<0.05). This finding is in contrast to recent studies that have investigated cardiovascular fitness variables and markers of HIV. In O'Brien's et al. (2017) meta-analysis, for example, five experimental studies examined peak VO_2 and markers of HIV, including CD4 T-cell count, nadir CD4 count, and HIV viral load. Consistently, studies showing improved peak VO_2 in PLWH had relative stability in markers of HIV. No direct relationship between these variables was observed. However, indirect relationships between these variables have been documented, particularly those related to chronic inflammation experienced by PLWH.[34]

Our results showed that PLWH had higher levels of the inflammatory cytokine IL-6 compared with controls, and that elevated IL-6 levels, were associated with fewer step per day and diminished peak VO_2 in PLWH. While inflammation is not unique to PLWH, HIV infection results in a state of elevated inflammation, particularly when HIV is poorly controlled. As such, higher levels of inflammation experienced by PLWH may play a role in their inability to achieve a similar peak VO_2 to controls. This may occur because elevated IL-6 is associated with increased fatigue, limiting how much PLWH can engage in physical activity and exercise. However, recent evidence suggests that physical activity may lead to decreased levels of inflammation,[46,47] which may, in part, account for improved peak VO_2 among PLWH who exercise. This evidence suggests that there is a complex interplay between factors that influence HIV disease progression, and its ultimate impact on cardiovascular health.

Limitations

Our study has several strengths including prospective data collection using objective measures of physical activity and cardiovascular fitness. However, we have several noteworthy limitations. First, as a cross-sectional study, we were unable to infer causality. Second, this is a single site study, and though we found novel, statistically significant relationships, our findings should be examined in a representative multi-site sample before implementing clinical changes based on our findings. Finally, although consistent with other studies, our results may reflect low levels of physical activity related to aging, as many of our participants were older adults living with HIV.

CONCLUSION

Increasingly, PLWH are aging and developing CVD. Given the complexities of HIV disease, non-pharmacological strategies to mitigate this CVD risk are needed. Physical activity is an evidence-based strategy known to prevent CVD. Our data demonstrate that aging PLWH have poor physical activity patterns and diminished cardiovascular health. Increasing the amount and intensity of lifestyle physical activity is likely to improve aspects of cardiovascular health in this population, especially cardiovascular fitness. However, the relationship between physical activity and cardiovascular health is complex and warrants further study.

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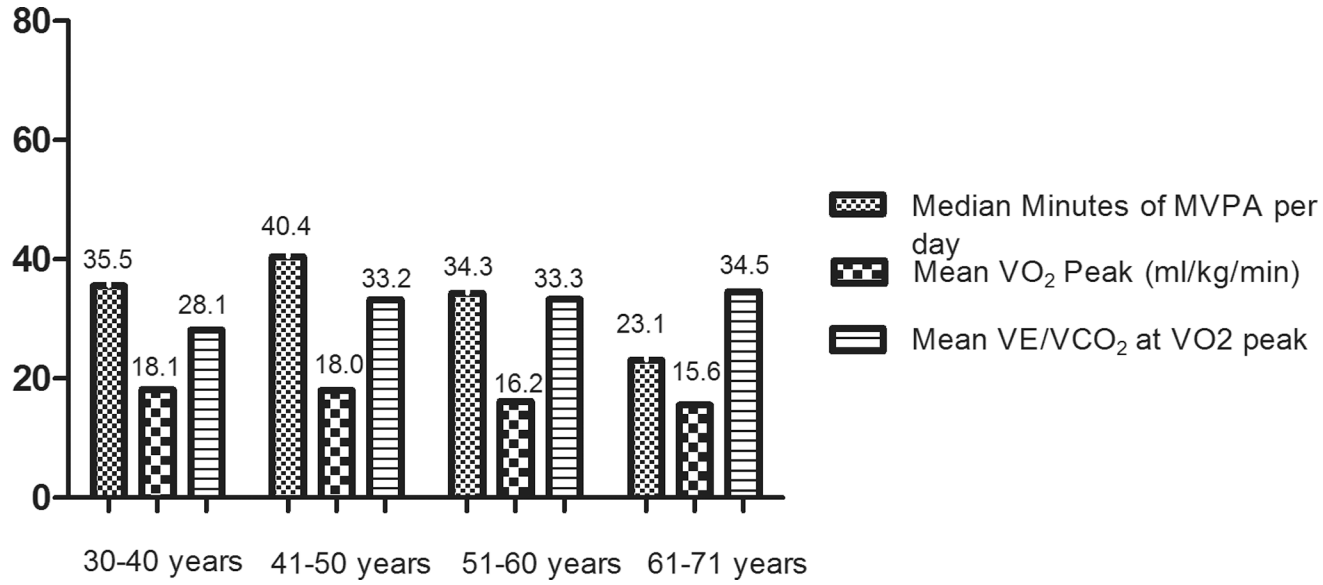

Figure 1.
Exercise and Fitness Characteristics of PLHIV

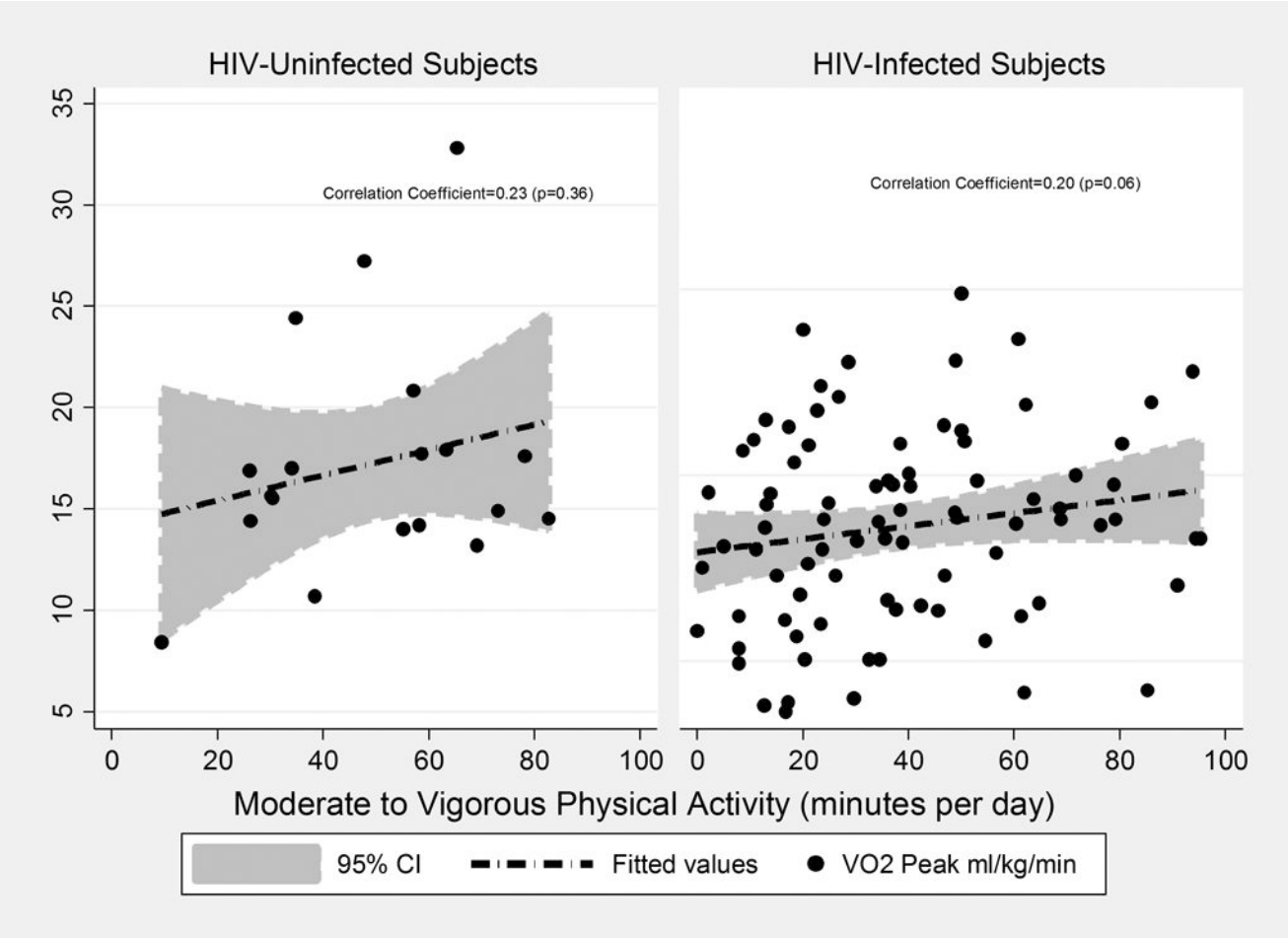

Figure 2.

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Table 1

Demographic, HIV, and Physical Activity Characteristics of the Sample

	HIV-Infected Subjects (*n*=109)	HIV uninfected subjects (*n*=20)	p-value[1]
Age in years (Range 31–71)	52.8 (7.27)	49.6 (6.86)	0.06
Male (%)[2]	70 (64)	12 (60)	0.70[3]
Race (%)			
African American	94 (86)	19 (95)	0.27[3]
Caucasian/White/Other	15 (14)	1 (5)	
Education (%)			
High School or less	56(51)	9 (45)	0.44[3]
Two years or less of college/advanced training	37 (34)	5 (25)	
College degree or higher	16 (15)	6 (30)	
Employed (%)	9(8)	7 (35)	<0.01[3,4]
Monthly Income			
>$600	20 (18)	5 (25)	0.83[3]
$600–999	54 (49)	9 (45)	
≥ $1000	34 (31)	6 (30)	
HIV and Inflammation Characteristics			
Years since HIV diagnosis	15.6 (7.74)	n/a	
Years taking HIV antiretroviral medication	12.5 (6.12)	n/a	
Current CD4+T cell count (cells/μL)	703.8 (404.4)	n/a	
CD4+T cell count nadir (cells/μL)	191.9 (170.0)	n/a	
Il-6	3.17 (2.46)	2.89 (1.81)	0.64
Median hsCRP (IQR)	1.75 (0.7, 4.3)	1.95 (0.9, 6.6)	0.37[3]
Physical Activity Characteristics			
Engaged in any moderate-to-vigorous physical activity during the past week	90 (83%)	19(95%)	0.20[3]
Steps per day	6,537 (3920)	7,040 (2265)	0.53
Median minutes of light physical activity (IQR) per day	753.6 (706,845)	752 (684,830)	0.73[3]

	HIV-Infected Subjects (*n*=109)	HIV uninfected subjects (*n*=20)	p-value[1]
Median minutes of moderate physical activity (IQR) per day	33.3 (17, 55)	47.8 (30,62)	0.05[3,4]
Median minutes of vigorous physical activity (IQR) per day	0 (0,0)	0 (0,0)	0.82[3]
Median minutes of moderate-to-vigorous physical activity (IQR) per day	35.1 (18, 58)	55.2 (31,65)	0.06[3]
Markers of Cardiometabolic Health			
VO_2 peak achieved (ml/min/kg)	16.77 (5.2)	16.85 (5.85)	0.94
Predicted VO_2 peak (ml/min/kg)	29.68 (15.58)	25.61 (7.46)	0.26
VO_2 peak at anaerobic threshold (ml/min/kg)	10.39 (4.04)	10.55 (2.94)	0.87
VE/VCO_2	33.10 (4.64)	30.2 (2.50)	0.03[4]
Percent Peak VO_2 at anaerobic threshold (VO_2 at AT/VO^2Max)	62%	63%	
Peak Work Achieved (watts)	93.6 (43.4)	111.35 (42.50)	0.09
Peak RER	1.07 (0.11)	1.08 (0.13)	0.70
Number of subjects achieving RER ≥ 1.0 (%)	84 (76)	17 (85)	0.56[5]
Median Coronary Calcium Score (IQR)	0 (0,66)	0 (0,170)	0.53[5]
Coronary Calcium Score >0 (%)	40 (36)	8 (40)	0.80[5]
Blood Pressure (mm Hg)	124/80	132/83	0.04[4]
Body Mass Index (kg/m^2)	29.3 (8.16)	32.5 (7.65)	0.11
Hip-Waist Circumference	0.94 (0.08)	0.94 (0.09)	0.72
Median HOMA-IR (IQR)	3.08 (1.7, 4.6)	3.81 (1.0, 5.6)	0.89

[1] Analyzed using T-tests, unless otherwise noted;

[2] There were 4 individuals who identified as transgender in the PLWH group and 1 in the control group;

[3] Due to the distribution of the data, differences between PLWH and controls were analyzed using Wilcoxon rank-sum tests;

[4] Difference between PLWH and control groups was ≤ 0.05;

[5] Frequency data were analyzed using Fisher's 2-sided exact statistic

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Table 2

Correlations between exercise, Immune characteristics, and markers of Cardiovascular health in people living with HIV[1]

	Step Counts	Moderate-to-vigorous physical activity	Il-6	CD4 + T cell Count(cells/μL)	CD4 + T cell Nadir(cells/μL)	VO_2 peak achieved (mL/kg/min)	VO_2 peak VE/VCO2
Step Counts per Day	1.0	0.81*					
Minutes of moderate-vigorous physical activity	**0.81[2]**	1.0					
Il-6	**−0.266[2]**	−0.111	1.0				
CD4 + T cell Count(cells/μL)	−0.074	−0.137	0.190	1.0			
CD4 + T cell Nadir(cells/μL)	0.070	−0.112	0.044	**0.404[2]**	1.0		
VO_2 peak achieved (ml/min/kg)	**0.342[2]**	**−0.204[2]**	**−0.257[2]**	**−0.199[3]**	0.010	1.0	
VO_2 peak VE/VCO2	0.060	−0.128	0.056	0.059	−0.014	−0.129	1.0
CAC score	0.172	0.121	0.202	−0.029	−0.115	−0.159	0.188
Systolic Blood Pressure	0.107	0.071	0.167	0.029	−0.010	0.026	−0.004
Diastolic Blood Pressure	0.100	0.146	0.120	0.00	0.016	0.096	−0.113
Total Cholesterol	−0.102	−0.121	−0.108	0.018	0.103	−0.185	0.140
HOMA-IR	**−0.215[3]**	−0.176	0.161	**0.248[2]**	0.033	**−0.327***	−0.072

[1] All associations were analyzed using Pearson Correlation Coefficient;

[3] p≤ 0.05;

[2] p≤ 0.01

Table 3

Quintile regression of physical activity and select covariates on peak VE/VCO_2

Covariates	β	SE(β)	p-value	95% Confidence Interval	
Physical Activity (30 minutes/day)	1.845	1.86	0.321	−1.83	5.523
HIV Infection	4.314	3.3299	0.198	−2.300	10.928
Age per decade	0.713	0.748	0.343	−0.772	2.198
Female	0.558	1.348	0.680	−2.119	3.236
Transgender	2.625	2.631	0.321	−2.601	7.851
Body-Mass-Index (kg/m^2)	−0.139	0.080	0.084	−0.298	−0.019
IL-6	0.139	0.263	0.597	−0.383	0.661
HIV × Physical Activity (30 minutes/day)	−1.944	1.932	0. 317	−5.781	1.893
Constant	27.309	5.721	<0.000	15.944	38.674